REMARKS/ARGUMENTS

Upon entry of this amendment, claims 64-76 and 78-83 will be pending in the application. Claim 75 is amended herein. Claim 77 is cancelled without prejudice to prosecution thereof at a later date. No new matter has been introduced by way of this amendment.

I. CLAIMS 64-76 AND 78-83 ARE ENABLED BY THE SPECIFICATION.

Claims 64-83 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. As best understood, the Examiner is of the view that he may reject the instant claims for lack of enablement in view of subsequent publications questioning whether Applicant's disclosed methods would work, notwithstanding undisputed, contrary evidence demonstrating that practice of the disclosed methods does, in fact, achieve the desired result. Applicant requests reconsideration of this rejection because the Examiner has failed to identify any legal authority supporting rejection on this basis, nor is Applicant aware of any.

The mere fact that a group of individuals have predicted that methods such as those claimed would not work is of no relevance to the enablement of the instant claims because there is undisputed evidence that such predictions were incorrect. Some level of skepticism as to advances in science and technology has always been raised, and probably always will. In fact, the magnitude of such skepticism is arguably proportional to the magnitude of the advance. In the final analysis, it is not relevant whether skeptics exist but, rather, whether they were right.

Here, the evidence of record clearly demonstrates that the skeptics that the Examiner has identified were *not* right. The invention as set forth in the application and as presently claimed has been proven to work in the years following the effective filing date of the present application. Indeed, clinical trials of antisense therapies have established that antisense technology does work in accordance with the principles and guidance set forth in the present application. For example, positive results have been obtained with the antisense drug Fomivirsen (Isis Pharmaceuticals, assignee of the present application), as substantiated by the approval thereof for the treatment of cytomegaloviral-induced retinitis by the FDA in 1998. Applicant further submits herewith a press release dated September 10, 2003 in which Genta

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Incorporated announced results of a successful Phase 3 clinical trial in which the effects of the antisense drug Genasense™ -- a compound that falls within the scope of the present claims -- against malignant melanoma were studied. (*See* Exhibit A attached hereto, available online at http://www.genta.com/Genta/InvestorRelation/2003/press_20030910_1.html.)

In short, no further disclosure other than that made by Applicant in 1981 was necessary for those skilled in the art to practice the inventions as presently claimed. This is the hallmark of enablement, and in no way is rebutted by the mere fact that there were those who doubted whether the underlying technology would ultimately be found to work. The methods that Applicant disclosed in 1981 have been demonstrated to work repeatedly thereafter. For these reasons and for those already of record which are hereby incorporated by reference, no clearer case of enablement can be shown. Accordingly, the rejection under 35 U.S.C. § 112 is improper and should be withdrawn.

II. THERE IS NO OBVIOUSNESS-TYPE DOUBLE PATENTING.

Claim 71 stands rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claim 1 of U.S. Patent No. 5,023,243. Applicant traverses.

In determining whether a nonstatutory basis exists for a double patenting rejection, the issue is whether any claim in the application defines an invention that is merely an obvious variation of an invention claimed in the patent. When the claimed subject matter is patentably distinct from the subject matter claimed in a commonly owned patent, a double patenting rejection is improper. *Eli Lilly & Co. v. Barr Labs.*, Inc., 58 U.S.P.Q.2d 1865 (Fed. Cir. 2001). Any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. § 103 obviousness determination (*In re Braat*, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991)); however, a double patenting rejection must rely on a comparison of only the claims. MPEP § 804, part III.

Claim 71 recites a method for selectively inhibiting the expression of a target protein in a cell producing messenger ribonucleic acids, the method comprising the steps of synthesizing a stabilized oligonucleotide having a sequence substantially complementary to a

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subsequence of a messenger ribonucleic acid coding for the target protein, introducing the stabilized oligonucleotide into the cell, and hybridizing the stabilized oligonucleotide to the subsequence of messenger ribonucleic acid to inhibit expression of the target protein, wherein the oligonucleotide is stabilized to inhibit degradation by nucleases.

In contrast, claim 1 of U.S. Patent No. 5,023,243 recites a method of selectively inhibiting *in vivo* synthesis of one or more specific targeted proteins comprising the steps of synthesizing an oligodeoxyribonucleotide having a nucleotide sequence substantially complementary to at least a portion of the base sequence of messenger ribonucleic acid coding for the targeted protein. In the claims of the '243 patent, at least a portion of the oligodeoxyribonucleotide is in the form of a phosphotriester to limit degradation *in vivo*. Claim 1 of the '243 patent calls for introducing the oligonucleotide into the cell and hybridizing the oligonucleotide to the subsequence of messenger ribonucleic acid to substantially block translation of the base sequence and to inhibit synthesis of the targeted protein. Claim 1 of the '243 patent does not render obvious claim 71 of the present application. No *prima facie* case of nonstatutory obviousness-type double patenting exists.

Applicant requests reconsideration and withdrawal of the rejection.

III. ALLEGED NEW MATTER

Claims 75-77 are rejected under 35 U.S.C. § 112, first paragraph, for alleged new matter. Applicant disagrees with the rejection. Nevertheless, in an effort to advance prosecution, Applicant has amended claim 75 to delete the alleged new matter. Applicant also has cancelled claim 77. Accordingly, Applicant requests withdrawal of the rejection.

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CONCLUSION

Applicant has presented claims that will give him the patent protection to which he is entitled. The present claims meet all requirements for patentability, and Applicant is entitled to issuance thereof. If the Examiner believes a telephone conference would expedite prosecution of this application, the undersigned may be contacted at 215-568-3100.

Respectfully submitted,

Date: September 17, 2003

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Attachments
Exhibit A

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